Efficacy and Safety of Risankizumab for Active Psoriatic Arthritis: 52-Week Results From KEEPsAKE 2

Andrew Östör[1], Filip Van den Bosch[2], Kim Papp[3], Cecilia Asnal[4], Ricardo Blanco[5], Jacob Aelion[6], Wenjing Lu[7], Zailong Wang[7], Ahmed M Soliman[7], Ann Eldred[7], Byron Padilla[7], Alan Kivitz[8]

[1]Monash University, Cabrini Hospital, Melbourne, Victoria, Australia; [2]Department of Rheumatology, Ghent University, Ghent, Belgium; [3]Probity Medical Research–K Papp Clinical Research, Waterloo, Ontario, Canada; [4]DOM Centro de Reumatología, Buenos Aires, Argentina; [5]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain; [6]Arthritis Clinic and West Tennessee Research Institute, Jackson, Tennessee, United States; [7]AbbVie Inc., North Chicago, Illinois, United States; [8]Altoona Center for Clinical Research, Duncansville, Pennsylvania, United States

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INTRODUCTION

- Interleukin 23 (IL-23) has been implicated in the pathogenesis of psoriatic arthritis (PsA)[1]
- Risankizumab (RZB), a humanized immunoglobulin G1 monoclonal antibody that specifically inhibits IL-23 by binding to its p19 subunit,[2,3] is approved to treat adults with moderate-to-severe plaque psoriasis[4] and is being investigated as a treatment for PsA
- The phase 3 RZB PsA program includes the following randomized, double-blind, placebo (PBO)-controlled trials:
  - KEEPsAKE 1: RZB vs PBO in adults with active PsA who have a history of inadequate response or intolerance to ≥1 conventional synthetic disease modifying antirheumatic drug (csDMARD-IR) therapy (NCT03675308)
  - KEEPsAKE 2: RZB vs PBO in adults with active PsA who have a history of inadequate response or intolerance to 1 or 2 biologic therapies (Bio-IR) and/or csDMARD-IR (NCT03671148)
- Primary (Week 24) results from KEEPsAKE1 and KEEPsAKE 2 demonstrated RZB 150 mg was well tolerated and significantly improves key clinical domains of PsA, including patient-reported outcomes and assessments of disease burden in patients who had previous inadequate response to csDMARDs and/or biologic agents[5,6] with a safety profile similar to that observed in patients with psoriasis[4]
- Week 52 results from KEEPsAKE 2 are presented here

OBJECTIVE

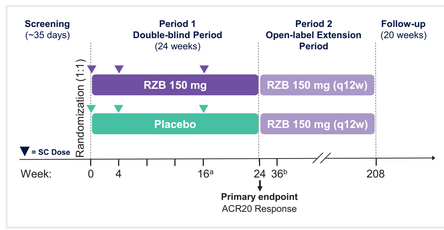
- Evaluate longer-term safety and efficacy of RZB 150 mg in patients with active PsA who experienced inadequate response or intolerance to 1 or 2 biologic therapies and/or to at least 1 csDMARD therapy

METHODS

STUDY DESIGN AND TREATMENT

- KEEPsAKE 2 is an ongoing, phase 3 study **(Figure 1)** that includes a screening period; a 24-week double-blinded, randomized, PBO-controlled, parallel-group period (Period 1); and an open-label extension period (Period 2)
- Period 2 started at Week 24, and all patients received open-label RZB 150 mg every 12 weeks through Week 208

Figure 1. KEEPSAKE 2 Study Design



[a]At Week 16, non-responders (patients not achieving ≥20% improvement from baseline in TJC and/or SJC at both Week 12 and Week 16) were eligible to add or modify rescue concomitant medications/therapy.
[b]Starting at Week 36, non-responders were discontinued from study drug.
ACR20, ≥20% improvement in American College of Rheumatology score; q12w, every 12 weeks; SC, subcutaneous; SJC, swollen joint count; TJC, tender joint count.

PATIENTS

- Aged ≥18 years
- Active PsA:
  - Symptom onset ≥6 months before screening
  - Meeting the Classification Criteria for PsA (CASPAR)
  - ≥5 tender (based on 68 joint counts) and ≥5 swollen joints (based on 66 joint counts)
  - Active plaque psoriasis (≥1 psoriatic plaque of ≥2 cm in diameter or nail psoriasis)
- Bio-IR and/or csDMARD-IR

EFFICACY ASSESSMENTS

- Proportion of patients who achieved
  - ≥20/50/70% improvement in American College of Rheumatology score (ACR20/50/70)
  - ≥90% reduction in Psoriasis Area Severity Index (PASI 90), among patients with ≥3% body surface affected by psoriasis at baseline
  - Minimal disease activity (MDA)
  - Resolution of enthesitis and dactylitis

METHODS (CONTINUED)

- Change from baseline in
  - Health Assessment Questionnaire Disability Index (HAQ-DI)
  - 36-Item Short Form Health Survey Physical Component Summary (SF-36 PCS) score
  - Functional Assessment of Chronic Illness Therapy-Fatigue Questionnaire (FACIT-Fatigue) score
- All efficacy outcomes were assessed at Weeks 24 and 52

SAFETY ASSESSMENTS

- Safety evaluations included adverse event monitoring, physical examinations, vital sign measurements, and clinical laboratory testing

STATISTICAL ANALYSES

- Efficacy and safety were assessed up to the Week 52 data cutoff (19 April 2021)
- Efficacy analyses were conducted on the full analysis set, which included all randomized patients who received ≥1 dose of study drug
- The primary Week 24 analysis used non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 (NRI-C) and a mixed-effect model for repeated measures considering intercurrent events
- Long-term Week 52 analysis used non-responder imputation (as observed with imputation) and mixed-effect model for repeated measures based on as observed data
- Safety analyses were conducted on the safety analysis set, which included all patients who received ≥1 dose of study drug
  - Treatment-emergent adverse events were summarized using exposure-adjusted event rates (EAERs, events/100 patient-years [PY])

RESULTS

PATIENTS

- Of the 443 patients who were randomized and dosed, 414 (93%) completed the PBO-controlled period and entered the open-label extension period
- Demographics and baseline disease characteristics were generally well balanced between groups **(Table 1)**

Table 1. Demographics and Baseline Disease Characteristics

Parameter	RZB 150 mg N = 224	PBO N = 219
Female, n (%)	124 (55.4)	120 (54.8)
Age, years, median (range)	53.0 (23–84)	52.0 (24–83)
BMI, kg/m^2, mean (SD)	31.5 (7.98)	31.2 (6.81)
PsA duration, years, mean (SD)	8.2 (8.24)	8.2 (8.29)
Swollen joint count,[a] mean (SD)	13.0 (8.73)	13.6 (8.89)
Tender joint count,[b] mean (SD)	22.8 (14.90)	22.3 (13.80)
BSA,[c] %, mean (SD)	12.5 (15.44)	11.7 (14.85)
PASI,[c] mean (SD)	7.74 (6.698)	8.35 (9.942)
HAQ-DI, mean (SD)	1.10 (0.618)	1.13 (0.626)
Presence of enthesitis,[d] n (%)	147 (65.6)	158 (72.1)
Prior biologics	105 (46.9)	101 (46.1)
Prior csDMARDs	212 (94.6)	208 (95.0)
Baseline csDMARDs	141 (62.9)	129 (58.9)
Baseline MTX[f]	110 (49.1)	99 (45.2)
Baseline oral corticosteroids	28 (12.5)	22 (10.0)
Baseline NSAIDs	141 (62.9)	145 (66.2)
No concomitant csDMARD at baseline	83 (37.1)	90 (41.1)

[a]Based on 66 joints.
[b]Based on 68 joints.
[c]Among patients with ≥3% BSA affected by psoriasis (RZB, N = 273; PBO, N = 271).
[d]Leeds Enthesitis Index >0.
[e]Leeds Dactylitis Index >0.
[f]As monotherapy or in combination with another csMARD.
BMI, body mass index; BSA, body surface area; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire-Disability Index; MTX, methotrexate; NSAIDs, non-steroidal anti-inflammatory drugs; PASI, Psoriasis Area and Severity Index; PBO, placebo; PsA, psoriatic arthritis; RZB, risankizumab.

RESULTS (CONTINUED)

EFFICACY

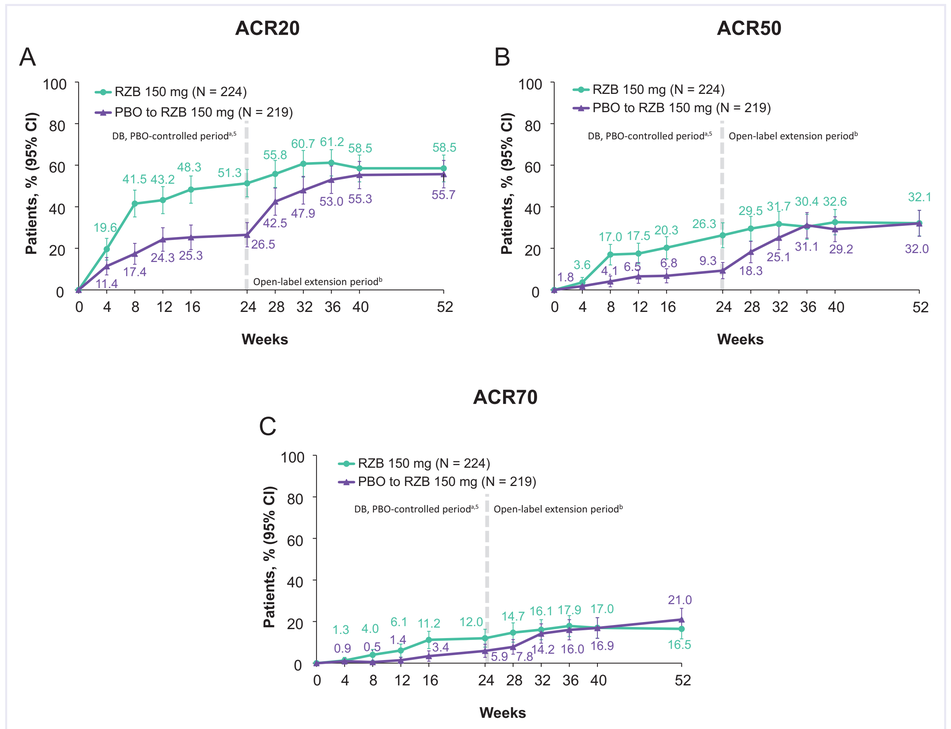
- At Week 24, a greater proportion of RZB-treated vs PBO-treated patients achieved ACR20 (51.3% and 26.5%, respectively; *P* <.001); efficacy was maintained at Week 52, and 58.5% of patients who were originally randomized to receive RZB and 55.7% of patients who were originally randomized to receive PBO and switch to RZB at Week 24 achieved ACR20 **(Table 2; Figure 2A)**
  - Similar results were observed for ACR50 **(Figure 2B)** and ACR70 **(Figure 2C)**, and other efficacy measures **(Table 2)**
- In patients with ≥3% of body surface area affected by psoriasis at baseline (N = 123 and N = 119 in RZB and PBO groups, respectively), 55.0% of RZB-treated patients and 10.2% of PBO-treated patients achieved PASI 90 at Week 24 (*P* <.001); 64.2% who were originally randomized to receive RZB and 59.7% who were originally randomized to receive PBO and switch to RZB at Week 24 achieved PASI 90 at Week 52 **(Figure 3)**

Table 2. KEEPsAKE 2 Efficacy Results

Parameter	Week 24[a] RZB 150 mg N = 224	Week 24[a] PBO N = 219	Week 52[b] RZB 150 mg N = 224	Week 52[b] PBO to RZB 150 mg N = 219
ACR20, n (%)	115 (51.3)	58 (26.5)	131 (58.5)	122 (55.7)
ACR50, n (%)	59 (26.3)	20 (9.3)	72 (32.1)	70 (32.0)
ACR70, n (%)	27 (12.0)	13 (5.9)	37 (16.5)	46 (21.0)
Change in HAQ-DI, mean (95% CI)	-0.22 (-0.28, -0.15)	-0.05 (-0.12, 0.02)	-0.26 (-0.32, -0.20)	-0.34 (-0.41, -0.28)
Resolution of enthesitis,[c] n/N (%)	63/147 (42.9)	48/158 (30.4)	64/147 (43.5)	83/158 (52.5)
Resolution of dactylitis,[d] n/N (%)	29/40 (72.5)	24/57 (42.1)	27/40 (67.5)	40/57 (70.2)
MDA, n (%)	57 (25.6)	25 (11.4)	61 (27.2)	74 (33.8)
Change in SF-36 PCS, mean (95% CI)	5.87 (4.86, 6.88)	2.01 (0.94, 3.08)	6.28 (5.22, 7.33)	7.30 (6.21, 8.39)
Change in FACIT-Fatigue, mean (95% CI)	4.9 (3.7, 6.0)	2.6 (1.4, 3.9)	5.7 (4.5, 6.9)	7.0 (5.8, 8.2)

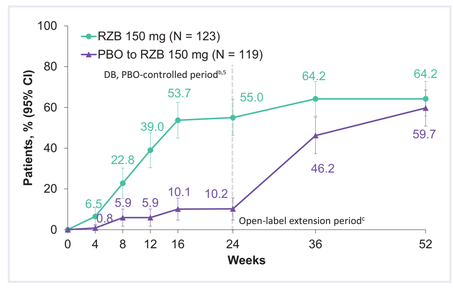
All changes are least square mean changes from baseline.
[a]Based on full analysis set, NRI-C.
[b]Based on full analysis set, NRI (as observed with imputation) was used for missing data.
[c]Among patients with Leeds Enthesitis Index >0.
[d]Among patients with Leeds Dactylitis Index >0.
ACR20/ACR50/ACR70, ≥20/50/70% improvement in American College of Rheumatology score; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy Fatigue Questionnaire; HAQ-DI, Health Assessment Questionnaire-Disability Index; MDA, minimal disease activity; NRI, non-responder imputation; NRI-C, non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19; PASI 90, ≥90% reduction in Psoriasis Area Severity Index; PBO, placebo; RZB, risankizumab; SF-36 PCS, 36-Item Short Form Health Survey Physical Component Summary.

Figure 2. ACR Responses Over Time



[a]Based on full analysis set, NRI-C.
[b]Based on full analysis set, NRI (as observed with imputation) was used for missing data.
ACR20/50/70, ≥20/50/70% improvement in American College of Rheumatology score; DB, double-blind; NRI, non-responder imputation; NRI-C, non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19; PBO, placebo; RZB, risankizumab.

Figure 3. PASI 90 Responses Over Time[a]



[a]Among patients with ≥3% body surface area affected by psoriasis at baseline.
[b]Based on full analysis set, NRI-C.
[c]Based on full analysis set, NRI (as observed with imputation) was used for missing data.
DB, double-blind; PASI 90, ≥90% reduction in Psoriasis Area and Severity Index; NRI, non-responder imputation; NRI-C, non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19; PBO, placebo; RZB, risankizumab.

SAFETY

- RZB was well tolerated through 52 weeks of treatment **(Table 3)**
  - EAERs of adverse events were stable between Weeks 24 and 52
  - At the Week 52 data cutoff, the total EAER of any TEAE in patients receiving RZB was 184.2/100 PY
- There were no deaths during the study

Table 3 Safety Events During Administration of RZB

Events (E/100 PY)	Week 24 N = 224 PY = 104.3	Long Term[a] N = 419 PY = 509.7
Any TEAE	286 (274.2)	939 (184.2)
Serious TEAE	14 (13.4)	48 (9.4)
TEAE leading to discontinuation of study drug	2 (1.9)	8 (1.6)
COVID-19–related TEAE	1 (1.0)	38 (7.5)
MACE	1 (1.0)	3 (0.6)
Serious infections	3 (2.9)	10 (2.0)
Active TB	0	0
Opportunistic infection excluding TB and herpes zoster	0	1 (0.2)
Herpes Zoster	0	3 (0.6)
Malignant tumors		
Including NMSC	1 (1.0)	11 (2.2)
Excluding NMSC	0	2 (0.4)
Anaphylactic reactions	0	0
Deaths	0	0

[a]Safety was reported through data cutoff date (19 April 2021) for both studies. Data are from any RZB 150-mg group that includes all patients who received RZB 150 mg, including those who started on RZB 150 mg at randomization and who switch from PBO to RZB 150 mg after Week 24.
TEAEs were defined as an adverse event with an onset date that is on or after the first dose of RZB and up to 140 days after the last dose of RZB if patient discontinued study drug prematurely.
E, events; MACE, major adverse cardiovascular events; NMSC, non-melanoma skin cancer; PBO, placebo; PY, patient-years; RZB, risankizumab; TB, tuberculosis; TEAE, treatment-emergent adverse events.

CONCLUSIONS

- Continuous RZB treatment maintained efficacy responses across multiple domains with a consistent safety profile through 52 weeks of treatment in patients with active PsA who were Bio-IR and/or csDMARD-IR
  - Similar efficacy result trends were also observed in patients initially randomized to PBO then switch to RZB at Week 24
- RZB was well tolerated, with a safety profile similar to that observed in patients with psoriasis and no new safety signals were identified[4]

DISCLOSURES

AÖ has received speaker or consulting fees and/or research grants from AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi, and UCB. **FVdB** has received speaker and/or consulting fees from AbbVie, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB. **KP** has received honoraria or fees for serving on advisory boards, as a speaker, and as a consultant, as well as grants as principal investigator from AbbVie, Amgen, Astellas, Bausch Health (Valeant), Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Coherus, Dermira, EMD Serono, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa Kirin, Lilly, LEO Pharma, MedImmune, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Stiefel, Sun Pharma, Takeda, and UCB. **CA** has received honoraria or fees for serving on advisory boards or as a speaker, as well as research support from AbbVie, Amgen, Genentech, Janssen, Lilly, Pfizer, Roche, and R-Pharm. **RB** has received grants or research support from AbbVie, Merck, and Roche. He has received consultation fees or honoraria for serving as a speaker for AbbVie, Bristol-Myers Squibb, Janssen, Lilly, Merck, Pfizer, and Roche. **JA** has received grants or research support from AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Galapagos/Gilead, Genentech, GlaxoSmithKline, Lilly, Mallinckrodt, Nektar Therapeutics, Nichi-Iko, Novartis, Pfizer, Regeneron, Roche, Sanofi, Selecta Biosciences, and UCB. **WL, ZW, AE,** and **BP** are full-time employees of AbbVie, and may hold AbbVie stock or stock options. **AMS** is a full-time employee of AbbVie, may hold AbbVie stock or stock options, and is a co-inventor on AbbVie patents. **AK** is a shareholder of or has received honoraria or fees as a consultant, speaker, or expert witness for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Flexion, Gilead, GlaxoSmithKline, Horizon, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB.

AbbVie Inc. participated in the study design; study research; collection, analysis, and interpretation of data; and writing, reviewing, and approving this poster. All authors had access to the data; participated in the poster's development, review, and approval; and made the decision to present this poster at the 3rd SDDS Congress.

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